REMARKS

Claims 1-8 and 10-19 are currently pending. Claims 4 and 18 have been cancelled without prejudice or disclaimer of the subject matter contained therein. Claims 1, 13, 15 and 19 have been amended to correct typographical errors and/or to obviate indefiniteness rejections. Support for the amendment to claims 1 and 15 may be found at page 21, line 10 *et seq.*, at page 19, lines 15-16, and in original claim 4. No new matter has been added.

1. Claim Objections

The Examiner has objected to claims 1, 13, 15, 18 and 19 because the word "re move"in step (e) should be –remove--. Applicants have reviewed the amended claims submitted in their last response and note that this typographical error only appeared in claims 1, 18 and 19 not in claims 13 and 15. Claim 18 has been cancelled but Applicants have made the appropriate correction in claims 1 and 19. Accordingly, reconsideration and removal of the objection is requested.

2. Claim Rejections under 35 U.S.C. §112, second paragraph

The Examiner has rejected claim 15 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner has rejected claim 15 as being indefinite because step (i) is incomplete and the phrase "the cation exchange resin of step (j)" lacks proper antecedent basis. Applicants have amended claim 15 to provide proper antecedent basis support for the cation exchange resin element in steps "k" and "j". Applicants have also clarified step (i) of claim 15. Applicants believe that the foregoing claim amendment has obviated the indefiniteness rejections. Reconsideration and removal of the rejection is respectfully requested.

3. Claim Rejections under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 13 and 15 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner argues that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner specifically states that "Claims 13 and 15 contain new matter in step (K) by virtue of referring to previous step (j), instead of (j), as in original claim 1". Applicants have amended step (k) in the referenced claims to refer to previous step (j) rather than (i).

The Examiner has also rejected claim 15 for containing new matter because step (i) did not refer to both an anion exchange resin and a cation exchange resin. As noted above, claim 15 has been amended and step (i) in claim 15 now corresponds to step (i) in claim 1. As such, the new matter rejection has been rendered moot. Reconsideration and removal of the rejection is respectfully requested.

4. Rejections under 35 U.S.C. §102

A. Doleschel et al.

The Examiner has rejected claims 1-8, 10 and 13-19 under 35 U.S.C. §102(b) as being anticipated by Doleschel et al.'s Product. In their previous response, Applicants have argued that numerous differences exist between the present products and those described in Doleschel. The Examiner has considered Applicants' arguments but was not persuaded. The Examiner argues that the instant products are not distinguishable from the Doleschel products because neither PEG content nor IgA are limitations in any of the claims. The Examiner further argues that even if PEG content was included as a limitation in the instant claims, the Doleschel products would still read on the invention because Doleschel teaches "removing PEG by ultra or diafiltration" and there are no limits with respect to the particular volume of buffer used for ultra or diafiltration. The Examiner then argues that Applicants' contentions with respect to the IgA

content of the Doleschel product are mere attorney argument unsupported by evidence. Applicants respectfully traverse.

The enclosed Declaration of Dr. Inga Laursen, a person of ordinary skill in the art, establishes that the Doleschel products contain high concentrations of unwanted PEG and IgA. The calculations presented in the Declaration demonstrate that the PEG content after ultracentrifugation against five times the volume of buffer will result in a product with a relatively high concentration of PEG. Furthermore, it illustrates that dialysis against at least 12 times the volume of buffer is needed in order to reduce the content of PEG to the levels taught by the present invention. Contrary to the Examiner's assertion, the particular amount of buffer used for ultra or diafiltration in the Examples is not "merely exemplary". To determine what it taught by Doleschel, one must examiner the entire reference. The paragraph bridging columns 3 and 4 clearly establishes that dialysis or ultracentrifugation against 5 times the volume of buffer is particularly preferred to remove the PEG from the IgG solution. Thus, one skilled in the art would reasonably believe that this volume is considered optimal. Given the fact that all of the Examples and the disclosure of the Doleschel reference teach the use of this particular amount of buffer to remove the unwanted PEG from the IgG solution, it is doubtful that one would believe that increased volumes of buffer could successfully be used to produce the Doleschel products. Accordingly, Applicants submit that the Doleschel products which would contain a PEG concentration of 3.125 mg/ml would not anticipate the instant products.

The Examiner has also rejected Applicants' arguments that the Doleschel products contained a higher unwanted content of IgA than the instant products and notes that claims 1, 15, 17 and 19 have no limitations regarding IgA content. Applicants would like to point out that the independent claims have been amended to include an IgA limitation which specifies that the IgA content of the claimed products shall be less than 6 mg/ml. In rejecting Applicants' previous argument, the Examiner had argued that the Doleschel products are "essentially free" of IgA and therefore read on the instant products. The IgA content of the Doleschel products were analyzed using the Ouchterlony method. Applicants had argued that this method shows a much lower sensitivity, at least 100 fold lower than the ELISA used for IgA quantification in the present

patent application. Thus, Applicant argued, the IgA content in the preparations of Doleschel, in reality, exceeds that of the products claimed in the present application.

The Declaration presents data from a supplementary experiment addressing the use of the Outcherloney technique for measuring the content of IgA. From the experimental data, it can be seen that even relatively high IgA concentrations of 50 mg/l could not be detected using this method. This data supports Applicants' arguments that the Ouchterloney technique is rather insensitive and cannot be used to substantiate the argument that the Doleschel immunoglobulin preparations are "essentially free" of IgA.

Finally, Applicants would like to point out that the independent claims 1 and 15 have been amended to recite that stabilizing agents are not added to the immunoglobulin product. Applicants believe that this limitation further distinguishes the present products from those described in Doleschel as the examples of Doleschel all require the addition of glycine as a stabilizing agent.

The foregoing remarks demonstrate the various differences between the instant products and those described by Doleschel. Applicants submit that these remarks are sufficient to rebut the Examiner's assumptions regarding the inherent teachings of Doleschel. Reconsideration and removal of the anticipation rejection in view of the Doleschel reference is, therefore, respectfully requested.

B. Mamidi et al. (US 6,162,904)

The Examiner has again rejected claims 1-2, 15, 17 and 19 under 35 U.S.C. §102(e) as being anticipated by Mamidi et al (US 6,162,904 and WO 99/33484) for reasons of record. Applicants had previously argued that the Mamidi product differs from the instant product because of differences in IgA and aggregates content. The Examiner withdrew the anticipation rejection with respect to claim 3 and its dependents but notes that claims 1 and 5 recite no limitations regarding IgA content. As noted above, Applicants have amended claims 1 and 15 to incorporate a limitation with respect to

IgA content and as amended claim 19 so that it now depends from claim 15. Applicants respectfully submit that the product of Mamidi is not consistent with the limits of claims 1 and 15 as amended. Applicants further submit that the claims as amended define over Mamidi and respectfully request removal and reconsideration of the anticipation rejection.

5. Rejections under 35 U.S.C. §103

The Examiner has rejected claims 1, 3 and 11-12 under 35 U.S.C. §103(a) as unpatentable over Mamidi or Doleschel alone or in view of Applicants' own admissions. The Examiner rejected Applicants' previous argument regarding the lack of stabilizers in the instant products because the claims contained no such limitation. Applicants respectfully traverse.

The amendments made to the claims and the foregoing remarks establish that the instant products are not anticipated by either the Doleschel or Mamidi references. Applicants further submit the instant products and method of the invention are not rendered obvious in view of the Mamidi or Doleschel references. As noted above, the claims have been amended so that products encompassed by the claims contain less than 6 mg/l of IgA and do not require the addition of a stablizer. As previously noted, the fact that the products of the invention do not need addition of stabilizers such as detergents, PEG or albumin, in order to avoid aggregation of IgG during storage was previously unknown and was not disclosed or suggested by any of the cited prior art references, either singly or in combination. The prior art products cited by the Examiner having a low content of polymers and aggregates all contain stabilizers as well as a high content of IgA and IgM. Thus, a IVIG product without said stabilizers and the use of these products to effectively treat various conditions would not be obvious to the skilled artisan. Reconsideration and removal of the obviousness rejection is respectfully requested.

Favorable consideration and early allowance of the claims is requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the

telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants hereby petition for an extension of time for one (1) months to December 26, 2003 for filing a reply to the Office Action dated November 26, 2002 in connection with the above-identified application. A check in the amount of $110.00 is enclosed.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____

Leonard R. Svensson, #30,330

P.O. Box 747
Falls Church, VA 22040-0747
(714) 708-8555

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on: Dec 29 2003
(Date of Deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

Susan Mangrum
(Signature)

Dec. 29 2003
(Date of Signature)